IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

KILEY WOLFE, Plaintiff, v. MCNEIL-PPC, INC.; MCNEIL CONSUMER & SPECIALTY PHARMACEUTICALS, a division of MCNEIL-PPC, INC.; MCNEIL CONSUMER HEALTHCARE, a division of MCNEIL-PPC, INC.; JOHNSON & JOHNSON, INC.; and JOHNSON & JOHNSON PHARMACEUTICAL AND RESEARCH DEVELOPMENT, LLC, Defendants.	CIVIL ACTION NO.: 07-0348 Judge: Jan E. DuBois

DEFENDANTS' TRIAL BRIEF

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Defendants, McNEIL-PPC, Inc., McNeil Consumer Healthcare Division of McNEIL-PPC, Inc. formerly known as and also sued as McNeil Consumer & Specialty Pharmaceuticals, a division of McNeil-PPC, Inc., Johnson & Johnson, and Johnson & Johnson Pharmaceutical Research and Development, LLC[1], submit the following Trial Brief:

I.

INTRODUCTION

This is a product liability failure-to-warn action regarding over-the-counter ("OTC") Children's Motrin that Plaintiff, Kiley Wolfe, ingested in May and June 1996. Plaintiff claims the Children's Motrin caused her to develop two rare medical conditions known as Stevens-Johnson Syndrome ("SJS")[2] and Vanishing Bile Duct Syndrome ("VBDS")[3], which caused injuries to her. Plaintiff claims Defendants are liable for her injuries under negligent and strict liability failure-to-warn theories because the Children's Motrin label was inadequate to warn of SJS and VBDS. Plaintiff seeks to recover punitive damages. Defendants do not dispute Plaintiff was injured in 1996, and has experienced a complicated medical history since that time. Defendants, however, deny OTC Motrin injured Plaintiff.

Plaintiff's claims fail because she cannot prove the threshold issue that Children's Motrin can cause SJS and VBDS (general causation) and cannot prove it caused SJS and VBDS in this case (specific causation). Plaintiff's claims also fail because the facts show the Children's

[1] McNeil Consumer Healthcare Division of McNEIL-PPC, Inc. manufactures and markets Children's Motrin. McNEIL-PPC, Inc. is an indirect subsidiary of Johnson & Johnson. Johnson & Johnson Pharmaceutical Research & Development, L.L.C. is also an indirect subsidiary of Johnson & Johnson.

[2] Defendants dispute that Plaintiff experienced SJS. SJS is an extremely rare and poorly understood disease affecting the skin and mucous membranes. It is marked by erupting blisters and sloughing of patches of skin. The initial symptoms are non-specific and include fever, sore throat, cough, or burning eyes. These symptoms are themselves conditions that are frequently treated with ibuprofen. The pathogenesis of SJS remains unknown, in part because it is so rare (1.2 to 6 cases of SJS per million persons per year, from all causes). Both infectious agents and medicines are both associated with the condition, and a percentage of cases are deemed idiopathic – their causes unknown.

[3] VBDS is an extremely rare form of liver disease manifested by the progressive destruction and disappearance of the liver's bile ducts. Bile is formed in the liver and aids in digestion; it is secreted by liver cells and collects in tiny canals called bile canaliculi which feed into the bile ducts. When the flow of bile is obstructed or the bile ducts are destroyed, it leads to a condition called cholestasis, resulting in a build-up of bile in the blood and jaundice.

Motrin label gave adequate warnings, and a different warning would not have made a difference. Among other things, Plaintiff's mother read only the dosing information when initially giving the medicine to Plaintiff; continued administering Children's Motrin to Plaintiff upon her doctor's advice, even after she allegedly studied the box and bottle that warned of the seriousness of the very symptoms Plaintiff was experiencing; had previously given Aleve to Plaintiff without reading the warning label on the product; gives Children's Motrin to her young sons even after Plaintiff's alleged reaction; and still uses ibuprofen herself.

Plaintiff has no evidence, let alone clear and convincing evidence, to support an award of punitive damages. Defendants' conduct was not motivated by ill will. Nor was Defendants' conduct in providing the Children's Motrin label at issue outrageous in light of the scientific discussion over whether Children's Motrin actually can cause SJS, the FDA's expressed view that ibuprofen may cause SJS although rarely, and the FDA's determination nevertheless that Children's Motrin was safe without a prescription and that OTC ibuprofen labels should not include an SJS warning.

II.

STATEMENT OF FACTS

A. Plaintiff Claims She Developed SJS and VBDS From Using Children's Motrin.

Kiley Wolfe was 9 years-old when – over 15 years ago – her mother gave her Children's Motrin. She became ill with a headache and stomach ache on May 26, 1996. The following day her symptoms worsened and she felt "bad." That day, her mother, Janet Leland, accepted an Aleve from a stranger in an airport and gave it to her daughter. Mrs. Leland did not review the medication bottle nor label before administering Aleve (a medication intended for use in adults); she merely looked at the pill to see that "Aleve" was written on it.

By May 28, Ms. Wolfe had developed a fever, and the next day her mother took her to see her pediatrician, Dr. Mulla. By this time, she was very sick with a rash, fever, headache, sore throat, swollen glands and another stomach ache. Dr. Mulla diagnosed Ms. Wolfe with a virus and recommended OTC Children's Motrin. Mrs. Leland immediately followed Dr. Mulla's

recommendation, purchased OTC Children's Motrin, and gave it to her daughter without reading any warnings or product information other than the dosing chart.[4] Mrs. Leland testified that she was concerned about giving her daughter Children's Motrin after Ms. Wolfe threw up the first dose and when her symptoms continued to worsen, so she called the doctor. According to Mrs. Leland, Dr. Mulla's office told her to continue giving the OTC Children's Motrin, and she did. Mrs. Leland trusted Dr. Mulla and the nurses at his office and relied on their recommendations to give additional doses of Children's Motrin.

Ms. Wolfe was admitted to Children's Hospital Boston on June 1. She still had a fever and her skin was blistering. Ms. Wolfe claims she was diagnosed with SJS, and that this SJS was associated with VBDS, which necessitated a liver transplant.

B. Children's Motrin Is Safe, Effective And Used By Millions.

The FDA approved OTC Children's Motrin for pain relief and fever reduction after it was determined to be safe and effective for those purposes. The active ingredient in Children's Motrin is ibuprofen, a propionic acid non-steroidal anti-inflammatory drug (referred to as a "propionic acid NSAID"). Ibuprofen is a commonly used drug, and is available as both a prescription and OTC medication. Since ibuprofen's introduction to the market in 1967, billions of doses have been sold worldwide. Since at least 1992, U.S. consumers alone have purchased more than 6 billion ibuprofen doses annually. This figure does not include the millions of doses provided by doctors and hospitals to patients each year.

C. Plaintiff's Claims.

On March 30, 2011, the Court granted Defendants' Motion for Summary Judgment on all claims except Plaintiff's claims for negligent failure-to-warn and strict liability failure-to-warn claims, and her claim for punitive damages. These are the claims remaining for trial.

[4] Mrs. Leland testified that she saw the instruction to shake the product well before use. That information is located on the back in bold just above the dosing chart – exactly where Mrs. Leland said she looked.

III.

DISCUSSION

A. Plaintiff Cannot Establish The Threshold Element Of Medical Causation.

A Plaintiff in a product liability case has the burden to establish she was injured as a result of using the product.[5] Plaintiff cannot establish Children's Motrin proximately caused her injuries.

In the most recent and robust study of potential drug causes of SJS—the EuroSCAR study[6]— ibuprofen was found not to have a statistically significant increased risk of developing SJS. After analyzing cases and controls from a population of more than 100 million from 1997 to 2001, the study concluded that ibuprofen and other propionic acid NSAIDs are "drugs of common use probably not associated with [SJS]." In reaching this determination, the authors noted several factors that should be considered in assessing the association of SJS and use of ibuprofen and other drugs. It was determined that a high proportion (50%) of ibuprofen users who developed SJS were also taking "highly suspect" drugs, and that those cases were far more likely caused by these other drugs. The study observed that ibuprofen and certain other drugs, which were often used to treat the early symptoms of SJS such as fever and malaise, had "doubtful association" with SJS (*i.e.*, were unlikely to be a cause of SJS). This study found a relative risk of 0.9 with a 95% confidence interval from 0.3 to 2.6. Both this multivariate and the univariate estimate of relative risk included 1 within the confidence interval and therefore were not statistically significant.

Despite EuroSCAR, Plaintiffs will undoubtedly argue the prior study and AERs—few in

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[5] *See Simon v. Wyeth Pharm., Inc.*, 989 A.2d 356, 368 (Pa. Super. Ct. 2009).

[6] *See* Maja Mockenhaupt, et al., *Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: Assessment of Medication Risks with Emphasis on Recently Marketed Drugs*, 128 J. Investigative Dermatology 35-44 (2008). This case control study evaluated a larger number of cases and controls with ibuprofen exposure than the earlier study performed by the same lead investigator – Maja Mockenhaupt, et al., *The Risk of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis Associated with Nonsteroidal Antiinflammatory Drugs: A Multinational Perspective*, The Journal of Rheumatology, 30:10, 2234-2240 (2003) ("SCAR"). The 2008 study reflects a more complete ascertainment of exposure history for ibuprofen than the SCAR study.

number as they may be[7]—are proof of a causal relationship. But the FDA has already stated that AERs are not reliable evidence of causation:

> A report or information submitted…under this section (and any release by FDA of that report or information) *does not necessarily reflect a conclusion by the applicant or FDA* that the report or information constitutes an admission *that the drug caused or contributed to an adverse effect*.

21 C.F.R. § 314.80(k) (2008) (emphasis added). Indeed, case after case confirms the FDA's assertion that AERs are not reliable evidence of causation.[8] The fact remains that the most robust scientific study to date did not find a statistically significant risk of developing SJS from ibuprofen, and Plaintiff cannot satisfy her burden to show use of Children's Motrin caused injury.

Nor is there evidence that ibuprofen causes VBDS. No studies have suggested a causative association. And despite billions of doses of ibuprofen used throughout the world for many years, there have been only a handful of cases ever reported in a patient with VBDS who has used ibuprofen, either alone or in combination with other drugs. Nor is there any evidence that these diseases are somehow associated. As McNeil's expert, Maja Mockenhaupt testified, in her 20 years studying SJS/TEN, inclusive of the approximately 3,000 patients in the German Registry for SJS/TEN, she has never seen a case of VBDS. McNeil itself has received only three reports of VBDS in persons using ibuprofen – including the report of Ms. Wolfe. And, including this case, there are only two reports in the literature of persons with VBDS and SJS/TEN.

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[7] As the FDA's Response to the Citizen's Petition explained in 2006, the agency's adverse event reporting system received only 49 reports over the course of 30 years of possible SJS or Toxic Epidermal Necrolysis (a more severe form of SJS) cases related to the use of all brands of ibuprofen.

[8] *E.g.*, *Black v. Food Lion, Inc.*, 171 F.3d 308, 313 (5th Cir. 1999) (case reports do not establish causal relationship); *McClain v. Metabolife Int'l, Inc.* 401 F.3d 1233, 1250 (11th Cir. 2005) ("Uncontrolled anecdotal information offers one of the least reliable sources to justify opinions about both general and individual causation."); *Casey v. Ohio Med. Prods.*, 877 F. Supp. 1380, 1385 (N.D. Cal. 1995) ("case reports are not reliable scientific evidence of causation, because they simply [describe] reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group; do not isolate and exclude potentially alternative causes; and do not investigate or explain the mechanism of causation").

B. Plaintiff Cannot Establish Motrin Caused Her Injury

Even if Plaintiff could somehow show ibuprofen can cause SJS and VBDS, the evidence proves ibuprofen did not cause her to experience these conditions here.

As discussed, before Plaintiff took any Children's Motrin, she was very sick with a rash, fever, headache, sore throat, swollen glands and a stomach ache. Her pediatrician, Dr. Mullah, diagnosed her with a viral illness, before recommending Plaintiff use Children's Motrin. Defendants' experts, Dr. Mockenhaupt and Dr. Fisher, agree it is more likely than not that a viral illness caused the illness Plaintiff experienced in May and June 1996.[9]

The conclusion that ibuprofen did not cause Plaintiff to experience SJS is additionally supported by studies showing a delay of at least four days between beginning of drug use and onset of an adverse reaction is the most suggestive timing supporting a drug cause of SJS. Putting aside the symptoms Plaintiff experienced before first using Children's Motrin on June 28, 1996, her continuing to experience a fever and developing blisters by July 1 further supports a finding that ibuprofen did not cause her to experience SJS.

C. Plaintiff Cannot Establish That A Different Label Would Have Made A Difference.

Moreover, in order to prevail on her failure-to-warn claims, Plaintiff must show that if a different and allegedly more adequate warning had been provided, Plaintiff would not have suffered her injuries. [10] Absent such proof, she cannot establish that Defendants' alleged failure to warn was the proximate cause of her injuries, and her claims fail as a matter of law.[11]

The facts show that different warnings would not have changed Mrs. Leland's conduct in May 1996: (1) she read only the dosing information when initially giving the medicine;[12] (2) her

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[9] Dr. Fisher further testified another infection may be responsible for Plaintiff's illness.

[10] *Demmler v. SmithKline Beecham Corp.*, 671 A.2d 1151, 1155 (Pa. Super. Ct. 1996) (quoting *Burnside v. Abbott Labs.*, 505 A.2d 973, 978 (Pa. Super. Ct. 1985) and *Mazur v. Merck & Co.,* 742 F. Supp. 239, 262 (E.D. Pa. 1990)); *see also Overbeck v. Cates,* 700 A.2d 970, 972 (Pa. Super. Ct. 1997). In the strict liability context, Plaintiff must prove that if a warning had been properly provided, the accident would have been avoided. *Berkebile v. Brantly Helicopter Corp.*, 337 A.2d 893, 902 (Pa. Super. Ct. 1975).

[11] *See Demmler*, 671 A.2d at 1155.

[12] Mrs. Leland also testified that she saw the instruction to shake the product well before use. That information is located on the back in bold just above the dosing chart – exactly where Mrs. Leland

doctor recommended it and she followed her doctor's recommendation; (3) she previously gave Plaintiff Aleve without reading the warning label; (4) her young sons use Children's Motrin even after Plaintiff's alleged reaction to it; and (5) she still uses ibuprofen.

Mrs. Leland testified that she "just double-checked the *dosage*" on the label before first administering the medicine to Ms. Wolfe. Additionally, her testimony reveals that no matter what the label warned, she listened to her doctor and the nurses who instructed her to continue to give Plaintiff Children's Motrin despite the fact that Plaintiff exhibited new symptoms and other symptoms warned of on the label. When she allegedly expressed initial doubts regarding using Children's Motrin, the doctor's office instructed her to continue giving it to Plaintiff and she did so. And when it appeared to Mrs. Leland that Plaintiff was having adverse reactions to the medication – **reactions explicitly warned of on the label such as "redness," "swelling," "rash," and "vomiting**" – the doctor's office instructed her to continue giving it and she did. The warning label on the Children's Motrin box is not a causal factor in this case because Mrs. Leland relied exclusively on Dr. Mulla and there is no evidence in the record to the contrary.

Furthermore, just days before this, Mrs. Leland gave Plaintiff an Aleve, another NSAID, that she obtained from a stranger in an airport. She never looked at that medication's warnings. Finally, even though Mrs. Leland claims that Plaintiff's use of Children's Motrin caused her daughter to suffer numerous life-threatening injuries (and thus, she is now aware of the alleged potential dangers of the medication), she continues to allow her young sons to be given Children's Motrin. She uses ibuprofen herself.[13]

D. <u>There Is No Clear And Convincing Evidence To Support An Award Of Punitive Damages</u>.

In the unlikely event Plaintiff establishes liability under her failure-to-warn theories, she

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said she looked.

[13] Because the warning that Plaintiff asserts should have been on the Children's Motrin label was considered and rejected by the FDA, Plaintiff's failure to warn claims are untenable for the independent reason that they are preempted by federal law. The Court denied Defendants' Motion for Summary Judgment on this basis. *See Wolfe v. McNeil-PPC, Inc.*, 773 F. Supp. 2d 561, 568-69 (E.D. Pa. 2011). Defendants preserve this issue for appeal.

cannot meet her high burden of proof to obtain punitive damages. To recover punitive damages in a product liability action under Maine law[14], a plaintiff must prove, *by clear and convincing evidence*, the existence of express or implied malice.[15] "Express malice" exists "where the defendant's tortious conduct is motivated by ill will toward the plaintiff."[16] "Implied malice" exists "where deliberate conduct by the defendant, although motivated by something other than ill will toward any particular party, is so outrageous that malice toward a person injured as a result of that conduct can be implied. . . . [S]uch 'implied' or 'legal' malice will *not* be established by the defendant's mere reckless disregard of the circumstances."[17]

Plaintiff's punitive damages claim rests on three charges: (1) Defendants sold an unsafe product; (2) Defendants failed to properly test Children's Motrin prior to offering it over-the-counter; and (3) Defendants failed to warn. Even if true – which they are not – none of these acts would constitute implied or actual malice supporting an award of punitive damages. To the contrary, there is "considerable doubt" that Children's Motrin causes SJS at all, and the FDA itself decided that Children's Motrin was safe without a prescription and specifically declined to include an SJS warning on OTC ibuprofen labels.[18] Indeed, as the Seventh Circuit recently emphasized, any "evidence of [Defendants'] negligence in selling Children's Motrin, with or without a prescription and with or without additional warnings, was slight"[19] – a conclusion equally applicable here, and which precludes a finding of malice.

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[14] On July 30, 2010, the Court entered an order that Maine law applies to Plaintiff's attempt to recover punitive damages.

[15] *Tuttle v. Raymond*, 494 A.2d 1353, 1361-63 (Me. 1985) (emphasis added).

[16] *Id.* at 1361.

[17] *Id.* (original emphasis); *see also*, *e.g.*, *Jordan v. Cap Quality Care, Inc.*, No. CV-04-248, 2009 Me. Super. LEXIS 78, at *24 (Me. Super. Ct. Mar. 16, 2009) (granting motion for summary judgment of plaintiffs' punitive damages claim because, "[e]ven if the defendants were grossly negligent, or even reckless, in administering adequate warning [for the drug product at issue], this does not constitute malice as required for an award of punitive damages").

[18] *Robinson v. McNeil Consumer Healthcare*, 615 F.3d 861, 868 (7th Cir. 2010); *see also* FDA's June 22, 2006 Response to Citizen's Petition at 9, Exhibit A to the Declaration of David F. Abernethy ("Abernethy Decl.").

[19] *Robinson*, 615 F.3d at 867.

Moreover, prior to seeking approval for OTC Children's Motrin, McNeil contracted with Boston University School of Medicine to conduct a large, double-blind, randomized controlled clinical trial of the safety of OTC ibuprofen for children ("BUFS"). The study was designed in conjunction with the FDA. It was, and still is, the largest (non-vaccine) prospective study in children ever designed and conducted. BUFS demonstrated the safety of ibuprofen for OTC children's use. A database containing patient data listings, including all health information and adverse reactions was provided to the FDA. The results of BUFS were also reported in a clinical study report, released on December 22, 1993, and the principal investigators presented the study in an article in the Journal of the American Medical Association in March 1995.[20]

The FDA has specifically rejected the accusation that McNeil withheld any material safety information.[21] And, the existence of medical literature, internal reports and adverse event reports associating ibuprofen with SJS is not evidence Defendants acted with fraud, malice and oppression. Over the years, McNeil has submitted to the FDA medical literature, case reports and other adverse event reports concerning SJS and ibuprofen. With knowledge of the scientific evidence, even as interpreted by Plaintiff's experts in a Citizen's Petition, the FDA concluded that the risk-benefit profile for ibuprofen remained very favorable and the product should continue to be available over-the-counter.[22] Courts have repeatedly found that the existence of a discussion or dispute over the safety of a product or a feature of the product is not a basis for punitive damages – rather, it is a defense to punitive damages.[23]

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[20] Defendants also contend Plaintiff's failure-to-warn claims are preempted because a state may not permit an award of damages for withholding information from the FDA, or otherwise misleading the agency. The Court denied Defendants' Motion for Summary Judgment on this basis. *See Wolfe*, 773 F. Supp. 2d at 576. Defendants also preserve this issue for appeal. *See Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001) (plaintiffs' state law fraud-on-the-FDA claims preempted because FDA has ample powers to punish and deter fraud against it).

[21] FDA's June 22, 2006 Response to Citizen's Petition, at 3, 5, 6, Exhibit A to Abernethy Decl..

[22] FDA's June 22, 2006 Response to Citizen's Petition, at 9, Exhibit A to Abernethy Decl.

[23] *See*, *e.g.*, *Satcher v. Honda Motor Co.*, 52 F.3d 1311, 1317 (5th Cir. 1995) (vacating punitive damages award based on the "genuine dispute in the scientific community as to whether leg guards do more harm than good"); *Burke v. Deere & Co.*, 6 F.3d 497, 511 (8th Cir. 1993) (reversing denial of JNOV because "[a]n award of punitive damages is not appropriate when room exists for reasonable disagreement over the relative risks and utilities of the conduct at issue"); *Hillrichs v. Avco Corp.*, 514

Plaintiff cannot meet her burden to demonstrate, by clear and convincing evidence, a basis to recover punitive damages.

IV.

CONCLUSION

For the foregoing reasons, Defendants respectfully submit judgment should be entered for Defendants.

Dated: August 22, 2011

Respectfully submitted,

/s David F. Abernethy

David F. Abernethy, Esquire
Pa. Attorney I.D. No. 36666
Kadene K. Chin, Esquire
Pa. Attorney I.D. No. 205968
DRINKER BIDDLE & REATH LLP
One Logan Square, Ste. 2000
Philadelphia, PA 19103-6996
(215) 988-2700 (Telephone)
(215) 988-2757 (Facsimile)

Attorney for Defendants
McNEIL-PPC, Inc., McNeil Consumer Healthcare Division of McNEIL-PPC, Inc., Johnson & Johnson, and Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

OF COUNSEL:

Thomas W. Pulliam, Jr., Esquire
Vernon I. Zvoleff, Esquire
Kenneth P. Conour, Esquire
Benjamin J. Holl, Esquire
DRINKER BIDDLE & REATH LLP
50 Fremont Street, 20th Floor
San Francisco, CA 94105
(415) 591-7500 (Telephone)
(415) 591-7510 (Facsimile)
thomas.pulliam@dbr.com
vernon.zvoleff@dbr.com
kenneth.conour@dbr.com
benjamin.holl@dbr.com

Christy D. Jones, Esquire
Kari Sutherland, Esquire
Michael B. Hewes, Esquire
Alyson Jones, Esquire
BUTLER SNOW O'MARA STEVENS & CANNADA, PLLC
Renaissance at Colony Park
1020 Highland Colony Parkway, Suite 1400
Ridgeland, MS 39157
601-948-4500 (Telephone)
601-985-4500 (Facsimile)
christy.jones@butlersnow.com
kari.sutherland@butlersnow.com
michael.hewes@butlersnow.com
alyson.jones@butlersnow.com

N.W.2d 94, 100 (Iowa 1994) (punitive damages are "inappropriate when room exists for reasonable disagreement over the relative risks and utilities of the conduct and device at issue").

CERTIFICATE OF SERVICE

I, Kadene K. Chin, hereby certify that on this day I caused a true and correct copy of Defendants' Trial Brief to be served via the Court's electronic filing system upon counsel listed below:

Joseph L. Messa, Esq.
Thomas N. Sweeney, Esq.
Brian P. Kelly, Esq.
MESSA & ASSOCIATES, P.C.
123 South 22nd Street
Philadelphia, PA 19103

Darryl J. Tschirn, Esq.
LAW OFFICES OF DARRYL J. TSCHIRN
7825 Fay Avenue, Suite 200
La Jolla, CA 92037

John M. Robin, Esq.
LAW OFFICES OF JOHN M. ROBIN
600 Covington Center
Covington, LA 70434

Dated: August 22, 2011

/s/ Kadene K. Chin
Kadene K. Chin